

AMENDMENTS TO THE SPECIFICATION:

Please replace the paragraph on page 2, lines 7-11 of the specification with the following:

The aforementioned foreign protein in the transformant according to the present invention should preferably be a bovine lactate dehydrogenase or its homologue. This protein would be especially effective if it were a protein consisting of the amino acid sequence shown in ~~sequence-number~~ SEQ ID NO:1, or its homologue. Furthermore, said protein should preferably be coded by the DNA sequence shown in ~~sequence-number~~ SEQ ID NO:3. This DNA sequence should preferably be held by the transformant as the DNA sequence shown in ~~sequence-number~~ SEQ ID NO:4.

Please replace the paragraph on page 2, lines 12-14 of the specification with the following:

The aforementioned promoter on the host chromosome should preferably be a pyruvate decarboxylase 1 gene promoter. Furthermore, this promoter should preferably use the DNA sequence shown in ~~sequence-number~~ SEQ ID NO:2 or its homologue.

Please replace the paragraph on page 3, lines 43-46 of the specification with the following:

The LDH should preferably be derived from a eucaryotic microbe such as yeast; and more preferably from a higher eucaryote, such as a plant, animal, or insect; and even more preferably from even higher eucaryotes, including mammals such as bovines. Bovine-derived LDH is the most preferable. An example of a bovine-derived LDH is the protein consisting of the amino acid sequence shown in ~~sequence-number~~ SEQ ID NO:1.

Please replace the paragraph on page 4, lines 10-13 of the specification with the following:

For example, a desirable homologue would be a protein with one or several amino acids in the amino acid sequence shown in ~~sequence-number~~ SEQ ID NO:1 replaced, void, inserted, and/or added, and which has LDH activity; or a

protein that is at least 70%, and more preferably at least 80%, homologous in its amino acid sequence to the amino acid sequence shown in ~~sequence number~~ SEQ ID NO:1, and which also has LDH activity.

Please replace the paragraph on page 6, lines 30-46 of the specification with the following:

It is preferable to use yeast to express the present DNA product, i.e., a protein having LDH activity; and therefore, the use of a promoter that expresses itself inside yeast is preferable. For such a promoter, it is preferable to use a pyruvate decarboxylase gene promoter, gal1 promoter, gal10 promoter, heat shock protein promoter, MF.alpha.1 promoter, PH05 promoter, PGK promoter, GAP promoter ~~promoter~~, ADH promoter, or AOX1 promoter, for example. In particular, a pyruvate decarboxylase 1 gene promoter derived from the ~~Saccaromyces~~ Saccharomyces family is preferable, and the use of the pyruvate decarboxylase 1 gene promoter derived from ~~Saccaromyces~~ Saccharomyces cerevisiae is more preferable. This is because these promoters are expressed at high degrees in the ethanol fermentation route of the ~~Saccaromyces~~ Saccharomyces family (cerevisiae). Note that said promoter sequence can be isolated using the PCR breeding method, which uses the genome DNA of the pyruvate decarboxylase 1 gene of a yeast in the ~~Saccaromyces~~ Saccharomyces family as the mold. The base sequence of said promoter derived from ~~Saccaromyces~~ Saccharomyces cerevisiae is shown in ~~sequence number~~ SEQ ID NO:2. For the promoter segment in the present DNA structure, it is possible to use a DNA comprised of the base sequence described in ~~sequence number~~ SEQ ID NO:2, as well as a DNA that is comprised of this base sequence with one or several bases void, replaced, or added, and which has promoter activity; or a DNA that is hybridized with a DNA formulated from some or all of the sequences in the base sequence shown in ~~sequence number~~ SEQ ID NO:2 or its complementary strand under stringent conditions and which has promoter activity (in other words, the homologue of said promoter).

Please replace the paragraph on page 10, lines 5-10 of the specification with the following:

A new DNA sequence (999 bp) for coding a protein having the LDH activity obtained based on the design guidelines in 2) through 5) above and by applying the frequently used codon in the codon usage shown in FIG. 1 (hereafter referred to as "LDHKCB gene") is shown in ~~sequence-number~~ SEQ ID NO:3. Additionally, a DNA sequence (1052 bp) that includes the DNA sequence shown in ~~sequence-number~~ SEQ ID NO:3, as well as the upstream side of its start codon and the downstream side of its stop codon (hereafter referred to as "LDHKCB sequence"), is shown in ~~sequence-number~~ SEQ ID NO:4.

Please replace the paragraph on page 10, lines 12-17 of the specification as follows:

In the DNA sequence shown in ~~sequence-number~~ SEQ ID NO:3, codons that were different from those used in the original DNA sequence were used in all amino acids except methionine. Note that the newly adopted codons were all frequently used codons from among those shown in FIG. 1. Furthermore, FIG. 2 shows the result of a computer-based homology analysis of the original bovine-derived LDH gene and the LDHKCB gene. As is clear from FIG. 2, it was discovered that a large number of replacements were needed over almost the entire DNA sequence.

Please replace the paragraph on page 10, lines 35-41 of the specification with the following:

A series of overlapping PCRs were carried out according to FIG. 3 to create the gene fragments that were ultimately targeted. The DNA sequences of all 28 primers shown in FIG. 3 (BA, B01, BB, B02, BC, B03, BD, B04, BE, B05, BF, B06, BG, B07, BH, B08, BI, B09, BJ, B10, BK, B11, BL, B12, BM, B13, BN, and B14) are shown in ~~sequence-number~~ SEQ ID NOS:5 through 32, respectively. After the base sequence of the synthesized LDHKCB gene was verified, a restriction enzyme process using EcoRI was applied. The sequence was then linked to the pCR2.1 TOPO Vector (Invitrogen), to which an enzyme process using EcoRI had been applied in a similar manner, using a normal method. This vector is referred to as the pBTOPO-LDHKCB vector.

Please replace the paragraph on page 11, lines 18-21 of the specification with the following:

A restriction enzyme BamH1 site was added to the PDC1P-LDH-U (31 mer, Tm value of 58.3°C.) end.

: ATA TAT GGA TCC GCG TTT ATT TAC CTA TCT C
(~~sequence number~~ SEQ ID NO:33)

A restriction enzyme EcoRI site was added to the PDC1P-LDH-D (31 mer, Tm value of 54.4°C.) end.

: ATA TAT GAA TTC TTT GAT TGA TTT GAC TGT G
(~~sequence number~~ SEQ ID NO:34)

Please replace the paragraph on page 11, lines 37-39 of the specification with the following:

A restriction enzyme XhoI site was added to the PDC1D-LDH-U (34 mer, Tm value of 55.3°C.) end.

: ATA TAT CTC GAG GCC AGC TAA CTT CTT GGT CGA
C (~~sequence number~~ SEQ ID NO:35)

A restriction enzyme ApaI site was added to the PDC1D-LDH-D (31 mer, Tm value of 54. 4°C.) end.

: ATA TAT GAA TTC TTT GAT TGA TTT GAC TGT G 4
(~~sequence number~~ SEQ ID NO:36)

Please replace the paragraph on page 13, lines 31-33 of the specification with the following:

LDG-KCB-U : TGG TTG ATG TTA TGG AAG AT (20 mer)
(~~sequence number~~ SEQ ID NO:37)

LDH-KCB-D : GAC AAG GTA CAT AAA ACC CAG (21 mer)
(~~sequence number~~ SEQ ID NO:38)

PDC1P-U3 : GTA ATA AAC ACA CCC CGC G (19 mer)
(~~sequence number~~ SEQ ID NO:39)

Please replace the paragraph on page 17, lines 20-22 of the specification with the following:

~~Sequence number~~ SEQ ID NO:3: Modified DNA for coding
Lactate dehydrogenase

~~Sequence number~~ SEQ ID NO:4: Modified DNA for coding
Lactate dehydrogenase

~~Sequence numbers~~ SEQ ID NOs:5 through 39: Primers